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SOME CASES ILLUSTRATING THE INFLUENCE OF HEREDITY IN ANGIO- NEUROTIC ŒDEMA.

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I PROPOSE in these notes to condense a medical family history which appears to me not only interesting in itself, but conclusive as to the hereditary character of a disease which I believe to be Angio-Neurotic Œdema.

I have definite information regarding eighty persons of this family, and of these thirty-three are or have been affected with the disease. Of the thirty-three twelve have died of suffocation, and of the remaining twenty-one some from other causes, whilst most of the surviving members of the family are under observation. Two doubtful cases are not included amongst the deaths.

Sex.—An analysis of the cases in this family shows that males are twice as frequently attacked as females, twenty-two being males and eleven females.

Age.—The disease generally commences in this family about the age of puberty, though in one case, that of Annie, daughter of Edwin, the child was only eight years old when first attacked. The ages of those who have died ranged from 16 years to 70 years. One patient was under 20, three were between 20—30, two between 30—40, and five between 60—70. I have been unable to ascertain the age of the remaining case, but am informed that she was over middle age.

In all the cases regarding which trustworthy information can be obtained, the symptoms and mode of onset are in fairly constant conformity with the description of the disease given in medical text-books.

Painless, frequently irritable, circumscribed swellings appear, with varying degrees of rapidity, on different parts of the body, generally on the arms, hands, legs or face; less often the mouth, tongue, or larynx are involved. It is worthy of note that almost all the affected members are peculiarly liable to severe intestinal colic.

The swellings disappear in some instances in from eight to twelve hours, though more frequently œdema is apparent for a much longer period, sometimes, I am told, for so long as forty-eight hours after the onset.

In the three following fatal cases I have seen the symptoms were almost identical, with the exception that in one of them there was much œdema of the face.

1.—Ezekiel L., æt. 66, was liable to sudden swelling in the throat and about the body. On October 16th, 1895, he was returning home from his work and at 3.50 p.m. was seen by a shepherd who spoke to him, and he then seemed in his usual health. At 4.5 p.m. he was found lying dead by the side of the road on the down a short distance from the spot where he stopped to speak to the shepherd. When I saw the body half an hour later it was lying prone, the hands clenched, and the face and visible mucous membranes were of a purplish colour. The tongue was not swollen. I was unable to obtain permission to make a post-mortem examination.

2.—Henry D., æt. 24, great nephew to Ezekiel L., had suffered from several attacks of œdema. On October 16th, 1895, he was sitting at his supper when he heard of his uncle's death. When told the cause he was much agitated and expressed the belief that he himself would die in the same way. He seemed a good deal upset at the suddenness of his uncle's end and spoke of it several times. Early on October 18th, 1895, I was called to him, and on arrival found him dead. He had been suddenly attacked with dyspnœa and was dead in a few minutes. His mother told me

that he had been several times threatened with suffocation. He would never go to sleep if his face was œdematous for fear it might spread to his throat.

3.—Sarah L., æt. 41, a niece of Ezekiel L., had since her girlhood been liable to attacks of localised œdema. On June 29th, 1891, whilst occupied with her household duties, her face became swollen. This was in the early afternoon, but, as she had previously been affected in the same way and recovered without the development of alarming symptoms, did not think much of it. As the œdema increased she went to her sister's house where she had tea. After tea she went upstairs and a few minutes later called out that "it was going to her throat and she was sure it would choke her." The face was then more swollen and the eyes were closed from the swelling. She was taken downstairs and the breathing rapidly became more laboured. She died suffocated a few minutes afterwards.

4.—The following case, that of Emily L., æt. 13, daughter of Henry L., suggests that the disease might attack lung tissue itself. She died cyanosed twelve hours after the onset of acute lung symptoms. I was called to see her on October 10th, 1895. A short time previously she complained of shortness of breath and became rapidly worse. The physical signs were those of acute bronchitis and there was moderate pyrexia. I could not determine whether any portions of the lungs were solid. The gravity of her condition increased, and she died the same evening. I gave a certificate ascribing death to acute capillary bronchitis, but it may fairly be asked if the condition might not have been one of angeio-neurotic œdema of the lungs sufficiently extensive to produce suffocation. The child had previously had attacks of localised œdema.

The following are the non-fatal cases I have seen :—

1a.—Eliza D., æt. 53, mother of Henry D., sent for me on October 21st, 1903, the messenger saying that she was suffocating. I found her sitting in an arm chair in some distress but apparently better than she had been. She could speak with difficulty. Her breathing was laboured but did not sound like that of laryngeal obstruction. The tongue was greatly swollen

*The Patient is the same as 11 &
page 116*

and watery looking and protruded between the teeth. I was informed that "it had been bigger but was going back now." The condition subsided in a few hours and when I saw her next day the tongue was normal in size. In this instance the tongue alone was affected. On November 7th, 1903, I called to make some further enquires regarding her family peculiarity and she was then recovering from another attack which had affected the left side of the face and temporal region. There was still some œdema over the malar bones, and puffiness of the eyelids. This condition had lasted about thirty hours.

2a.—Henry L., æt. 50, father of Emily L., has frequently had swelling in the throat and about the body. I attended him in March, 1897, for severe intestinal colic. There was no œdema externally. The pain was so severe as to require opium for its relief. He tells me that he has had many attacks of colic since, but never so severe as to need treatment. He has many times had swellings in the throat and on three occasions has been threatened with suffocation. The last of these occurred whilst he was under treatment in Salisbury Infirmary for another condition in 1897. The treatment adopted was ice poulticing which was kept up for twelve hours, after which the œdema subsided.

I have obtained the subjoined information regarding the following cases, either from the patients themselves or their near relatives, and I have no reason to doubt the accuracy of what they have told me:—

1b.—Luke L., æt. 70, was the first member of the family to be affected so far as is known. He was liable to swellings on various parts of the body, and was found lying dead on the floor in his house in 1843.

2b.—William L., æt. 70, was often attacked with the disease but did not die of it. His nephew, Edwin, tells me that he usually had attacks of intestinal colic every ten days. They began with pain in the abdomen and were always followed by vomiting. Independently, he would get the characteristic swellings about his body. These attacks of colic lasted, as a rule, about twelve hours.

3b.—Lot L., æt. 61, died May 7th, 1856, of an acute abdominal disease. He was taken suddenly ill with pain in the stomach and vomiting and died in twenty hours. His son tells me that the doctor said death was due to inflammation of the stomach. This man, like his brother, suffered much from colic, which was also periodical and came on every nine days, in addition he was frequently attacked with localised œdema.

4b.—Edwin L., æt. 68, son of Lot, tells me that he used to suffer severely, but for the last three or four years has been comparatively free. The hands and feet are most often affected now, but earlier in life he was very subject to abdominal pain and vomiting. These would last twelve to twenty-four hours. He has had many attacks of swelling in throat and mouth. On one occasion, ten or twelve years ago, he “made up his mind that he was going to choke.”

5b.—Richard L., æt. 22, used to have swelling in throat. He enlisted in the Grenadier Guards and died May 2nd, 1853, during an attack. This man was brother to Edwin.

6b.—Annie L., æt. 16, daughter of Edwin. Had many attacks, the first when eight years old. During the evening of April 15th, 1883, one of her hands became swollen. She went to bed and slept, but woke in the early morning as she felt she was choking. The difficulty in breathing increased, and she died suffocated one and a half hours later. Her father tells me that the features looked quite natural after death.

7b.—William L., æt. 66, had an attack of œdema of hands on May 24th, 1892. It began in the early morning, but he went to his work as usual and did not pay much attention to it. He returned home about mid-day as his throat was becoming affected. A doctor was sent for, but he died of suffocation at 1.45 p.m., before help had arrived. His daughter Sarah tells me that the doctor said his life could have been saved by tracheotomy had he been seen early enough. This patient was very liable to colic and had often been affected with swellings about the face and hands. His daughter says she has frequently seen his face so swollen that he could not see. She herself is free and has nine children, none of whom suffer from the disease.

8b.—James L., æt. 60, died at Hereford on January 22nd, 1901, of œdema of larynx. I have no details regarding his illness beyond the fact that his sister, Elizabeth D., received a letter the following day saying that he had been taken ill with swelling in the throat and had been suffocated.

9b.—Thomas L., æt. 38, brother of James L., was also subject to œdema. He was walking home from his work in March, 1885, and was found sitting by the roadside gasping for breath. He was able to say that his throat was swelling, and a few minutes afterwards died.

10b.—Henry L., æt. 64, father of Elizabeth D., was affected but did not die of the disease. His daughter says that he had many attacks in the throat and on the hands, face and about the body. He suffered from colic. On one occasion in 1883 he was asleep in bed when he was threatened with suffocation. He sprang up and had to be restrained from rushing out of the house. The attack lasted for about three minutes before he was able to get his breath again.

11b.—Elizabeth D., æt. 55, daughter of the last-named patient, tells me she has been liable to the disease so long as she can remember. She thinks her mouth or throat must have been swollen fifteen or twenty times. She does not always feel as though she would choke. When her throat is affected she says there is generally œdema of the neck as well.

12b.—Francis D., æt. 27, daughter of Elizabeth D., suffers from swelling of the hands, and has had three attacks in the throat.

13b.—Edith D., æt. 29, and 14b, Katharine D., æt. 25, are both affected but have never been threatened with suffocation.

15b.—Lucy L., æt. 18, daughter of Sarah L., had her first attack in her hands in November, 1899. Since then she has three times been affected, once her hand became swollen, and twice the face was œdematous.

16b.—James L., æt. 26, brother of Sarah G., died of suffocation on October 16th, 1883. He had several times been affected with œdema of the hands, but the throat had never been swollen before his fatal attack.

The cases may be divided into four groups—

1. In which the subcutaneous tissue alone is affected.
2. In which the mucous lining of the air and alimentary passages are primarily involved.
3. A combined form in which the œdema commences on the face and spreads thence to the buccal and laryngeal mucous membranes.
4. A condition in which intestinal colic is present without any external sign of œdema.

Groups 1 and 4 are the commonest and least dangerous forms of the disease, and the patients do not usually pay much attention to it when so affected, so that opportunities for watching the development of the attacks are rare; it is only when suffocation threatens that they send for medical help and then generally too late for assistance to be of any avail.

In group 2, the onset is more often quite sudden, and unless the swelling quickly subsides death ensues in a few minutes. Cases 1, 2, 1b, 6b, 7b, 9b and 16b, are examples of this form of the disease.

In group 3, the condition commences more gradually, and suffocation does not take place unless the œdema spreads to the larynx. Elizabeth D., No. 11b, may be taken as a non-fatal example of this condition; and Sarah L., No. 3, as a fatal instance.

The cases suggest several interesting considerations:—

1. *Medical*.—In a condition so rapidly fatal as sudden œdema of the larynx has proved to be, the question of treatment both preventive and immediate is of importance, for it can only be by chance that medical aid can be at hand in time to perform the necessary tracheotomy. My father, who had seen many of the cases, used to treat them with drachm doses of tinctura ferri perchloridi, repeated if necessary every twenty minutes, and he has told me that this has, in several instances, seemed of value. Elizabeth D., No. 11b, tells me she was under his care during an attack of threatened suffocation, and thinks that the drug saved her life. She described its effect as “cutting a way for

the air." The forms of treatment adopted by the patients themselves are as varied as they are curious:—Edwin L., No. 4b, says he used regularly to take a tablespoonful of sulphur every week and that this seemed to lessen the frequency and severity of his attacks. When his mouth was swollen he says that "the rough medicine did him good." It was my father's practice to keep those who were liable supplied with the iron mixture in case of emergency. Henry L., No. 2a, tells me that when his throat or mouth begins to swell he keeps sucking pieces of salt butter which relieves him. He does not think that the iron mixture has much effect. His daughter informs me that Henry L., No. 10b, when attacked in the throat would always keep walking about in the open air, for he could breathe more easily whilst "on the move."

2. *Social*.—From a social standpoint the question as to whether persons liable to angeio-neurotic œdema should marry, is not unimportant. So far as the history of this particular family may be taken as a guide, it certainly indicates that they should not. Many of the survivors of the present generation are either childless or too young to marry. Probably, however, some of them will in due course transmit their unfortunate tendency to their offspring, who will be, as their predecessors have been, the inheritors of a legacy which will very likely be fatal to them sooner or later.

3. Another question arises in connection with Life Insurance. What should be the medical examiner's recommendation to an Insurance Company when reporting on the life of a person known either to be affected with angeio-neurotic œdema or to belong to a family in which the disease has appeared?

The history of this family shows that the disease has already killed practically 35 per cent. of those affected and, if these figures are of any value, they indicate that the lives are uninsurable or should be so heavily loaded as to make it improbable that the insurance would be completed.

4. *Medico Legal*.—In the case of persons found dead the point might be raised whether death resulted from foul play.

5. *Conclusion.*—These cases, although too few in number to allow safe conclusions to be drawn from them, seem to indicate :—

1. That the disease is commoner in males than in females.
 2. That it occurs at all ages, but seldom before puberty.
 3. That the tendency to recurrence remains throughout life.
 4. That when the larynx is affected the condition is a very fatal one.
 5. That members of an affected family who themselves escape are less liable to transmit the disease to their children than those who are affected.
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